# The chromatin regulator Brg1 suppresses formation of intraductal papillary mucinous neoplasm and pancreatic ductal adenocarcinoma.

**Journal:** Nat Cell Biol

**Publication Year:** 2014

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**PubMed link:** 24561622

**Funding Grants:** Training Program in Stem Cell Research at UCSF

**Public Summary:**

**Scientific Abstract:**
Pancreatic ductal adenocarcinoma (PDA) develops through distinct precursor lesions, including pancreatic intraepithelial neoplasia (PanIN) and intraductal papillary mucinous neoplasia (IPMN). However, genetic features resulting in IPMN-associated PDA (IPMN-PDA) versus PanIN-associated PDA (PanIN-PDA) are largely unknown. Here we find that loss of Brg1, a core subunit of SWI/SNF chromatin remodelling complexes, cooperates with oncogenic Kras to form cystic neoplastic lesions that resemble human IPMN and progress to PDA. Although Brg1-null IPMN-PDA develops rapidly, it possesses a distinct transcriptional profile compared with PanIN-PDA driven by mutant Kras and hemizygous p53 deletion. IPMN-PDA also is less lethal, mirroring prognostic trends in PDA patients. In addition, Brg1 deletion inhibits Kras-dependent PanIN development from adult acinar cells, but promotes Kras-driven preneoplastic transformation in adult duct cells. Therefore, this study implicates Brg1 as a determinant of context-dependent Kras-driven pancreatic tumorigenesis and suggests that chromatin remodelling may underlie the development of distinct PDA subsets.